REMARKS

Rejections for double-patenting and for obviousness under 35 U.S.C. §103

Claims 1-5, 8, 10-12, 14-16 and 20-23 have been rejected under the judicially created doctrine of obviousness-type double patenting as being obvious over claims 1, 2, 4-7, 12-13, and 15-19 of U.S. Pat. No. 5,952,176 (hereinafter referred to as "U.S. '176") in view of Chirikjian et al., U.S. Pat. No. 5,656,430 (hereinafter referred to as "U.S. '430"). Claims 1-2 and 8-23 have been further rejected under 35 U.S.C. §103 as being obvious over WO 97/03210 (the PCT International Publication corresponding to the U.S. '176 patent, hereinafter referred to as WO '210) combined with U.S. '430. Applicants traverse these rejections and withdrawal thereof is respectfully requested.

In response to Applicant's arguments of November 26, 2001, the Examiner asserts that recitation of "an additional template" in claim 1 is not clear and therefore gives no patentable weight to the claim. Claim 1 has been amended for clarity to recite in step iv):

> iv) incubating the released extendible upstream DNA fragment in the presence of an enzyme allowing for extension thereof and **a template nucleic acid, which has partial or full sequence complementarity to the upstream fragment** and analysing resultant fragment(s).

Support for this amendment may be found on page 21 of the specification. Thus, the present invention is drawn to a method for characterizing nucleic acid molecules by

i) introducing a modified base which is a substrate for a DNA glycosylase into a DNA molecule;

ii) excising the modified base by means of said DNA glycosylase so as to generate an abasic site;

iii) cleaving the DNA at the abasic site so as to generate and release an extendible upstream DNA fragment having a 3′ hydroxyl terminus; and

iv) incubating the released extendible upstream DNA fragment in the presence of an enzyme allowing for extension thereof and a template nucleic acid, which has partial or full sequence complementarity to the upstream fragment and analysing resultant fragment(s).

The method of the present invention differs from the disclosed methods of U.S. '176/WO '210 and U.S. '430 such that even when the references are combined, steps of the invention are missing from the teachings of the references. The invention is thus not obvious for purposes of obviousness-type double patenting or obviousness under 35 U.S.C. §103.

The presently claimed invention differs from the disclosure of U.S. '176/WO '210 in that the references fail to teach steps iii)

and iv) of the present invention. Specifically, there is no disclosure in U.S. '176/WO '210 of specifically cleaving the DNA at the abasic site so as to generate an extendible DNA fragment having a 3' hydroxyl terminus or of the addition of a template nucleic acid, which has partial or full sequence complementarity to the upstream fragment and analysing resultant fragment(s). As indicated on page 2, lines 1-6, of the specification, the assay method of U.S. '176/WO '210 has the disadvantage of not being able to simultaneously analyze multiple samples. The method of the present invention, by the use of the features of steps iii) and iv) overcomes the disadvantages associated with U.S. '176/WO '210 and permits the simultaneous analysis of multiple samples.

The present invention is not achieved if U.S. '176/WO '210 is then combined with U.S. '430. U.S. '430 differs from the present invention in failing to disclose step i) - the introduction of a modified base. In addition, U.S. '430 fails to disclose step ii) of the invention because while U.S. '430 discloses the use of glycosylase enzymes, the glycosylases of U.S. '430 recognize normal nucleic acid bases, not modified bases. Thus, the glycosylase enzymes of US '430 would not achieve step ii) of the invention. Finally, U.S. '430 fails to disclose step iv) of the present invention, i.e. the addition of a template nucleic acid, which has partial or full sequence complementarity to the upstream fragment

and analysing resultant fragment(s). Thus, even if U.S. '176/WO '210 and U.S. '430 are combined, the present invention is not achieved because the combined references fail to disclose step iv) of the present invention. As such, the invention is not obvious over the references either for purposes of obviouness-type double patenting or 35 U.S.C. §103. Withdrawal of the rejection is therefore respectfully requested.

Claims 3-7 further remain rejected as being obvious over WO '210 combined with U.S. '430 and Dianov et al. Dianov et al. merely disclose DNA repair mechanisms and the use of DNA polymerases to repair a damage site. Dianov et al. fail to disclose at least either of steps i) or step iv) of the present invention. As such, Dianov et al. fails to make up for the deficiencies in the teachings of U.S. '176/WO '210 and U.S. '430 and the present invention is not achieved by combining the references. Withdrawal of the rejection is therefore respectfully requested.

Rejections under 35 U.S.C. §112, second paragraph

The Examiner maintains the rejection of claim 19 as being unclear in the meaning of "the reporter oligonucleotide is partially degenerate." Applicants traverse this rejection and

withdrawal thereof is respectfully requested. Applicants explained in the response of November 26, 2001, the accepted meaning of "partially degenerate."

As further indicated in the interview, the degree of degeneracy is experiment dependent and one skilled in the art would readily know how much degeneracy is desirable depending on the particular analysis being run. For example, the reporter oligonucleotide would typically have degeneracy at up to 50% of the nucleotide position or a typical reporter oligonucleotide of approximately 40 nucleotides in length could contain up to 20 degenerate nucleotides at the 5' end with the remainder of the being of a specific nucleotide sequence. As such, the degree of degeneracy is variable depending on the particular experiment and it would be improper to define an absolute degree of degeneracy in claim 19.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD (Reg. No. 40,069) at the telephone number of the listed below.

A marked-up version of the amended claim showing all changes is attached hereto.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a two (2) month extension of time for filing a reply in connection with the present application, and the required fee of $200.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachments

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Claim 1 has been amended as follows:

1. (Twice Amended) A method for characterising nucleic acid molecules, which comprises the steps of:

i) introducing a modified base which is a substrate for a DNA glycosylase into a DNA molecule;

ii) excising the modified base by means of said DNA glycosylase so as to generate an abasic site;

iii) cleaving the DNA at the abasic site so as to generate and release an extendible upstream DNA fragment having a 3' hydroxyl terminus; and

iv) incubating the released extendible upstream DNA fragment in the presence of an enzyme allowing for extension thereof and ~~an additional~~ a template nucleic acid, **which has partial or full sequence complementarity to the upstream fragment** and analysing resultant fragment(s).